Reviewer's report

Title: Reinterpretation, reclassification, and its downstream effects: Challenges for clinical laboratory geneticists

Version: 0 Date: 20 Sep 2019

Reviewer: Danya Vears

Reviewer's report:

This study utilised an online focus group of participants from Dutch laboratories to explore their practices and views on reinterpretation of genomic sequence data. This is an important topic which has been underexplored in the literature, the paper is well written, and the methodology appears sound. I have the following comments:

Abstract
The authors should list in the abstract how many Dutch laboratories were represented (not everyone knows how many labs there are in the Netherlands) and also how many laboratory geneticists participated in the focus groups.

Introduction
Line 35 - "This influx of genomic information not only leads to an increased diagnostic yield, but also results in a continuous redrawing of connections between genetic variants and genetic conditions". This sentence requires a reference.
Line 62 - Again, it would be good to state how many Dutch laboratories were represented.
Line 63 - "...the authors intend to identify key issues and concerns...". This wording is a bit strange. It implies that the authors will do this in the future but have not done it yet. Consider rephrasing.

Methods
Line 80 - "A qualitative research format was chosen...". I am not clear what the authors mean by this. Please elaborate.
Line 106 - I think you can remove "(the authors)". This is implied.
Was the information in Table 2 provided as case studies for participants to react to? How were these used? Were there other case studies as well? Please clarify.

Results and discussion
Line 187 - "Concerns existed among laboratory geneticists regarding the autonomy of these patients, as well as the durability of consent." Was there any discussion of whether the laboratory consent forms addressed reinterpretation?
Line 209 - "They may feel a moral responsibility to act on new information, after it has been generated." Are you suggesting that they do not feel an obligation to act on reactive classifications? Yet they generally reissue reports if a variant is reclassified reactively, right? Please clarify.
Line 242 - "participants pointed out." This is implied and can probably be deleted.
Line 249 - "Our focus group discussion showed that laboratory geneticists feel the clinician is responsible for establishing what is clinically significant." I am a bit unclear how this is achieved…

Table 3 - Consider shading the middle boxes, rather than marking with an X to avoid confusion (eg. X could also be misconstrued as a no).

Line 290 - It may be helpful to provide information about the increased diagnostic yield associated with reanalysis.

Line 354 - The expression is "gold standard".

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

Yes

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Unable to assess

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

Yes

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

Not relevant to this manuscript

**Quality of written English**
Please indicate the quality of language in the manuscript:

Acceptable

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